



SEQUENCE LISTING

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<120> CRYSTAL STRUCTURE OF BACE AND USES
THEREOF

<130> 16163-015001

<140> US 09/955,737

<141> 2001-09-19

<150> US 60/234,576

<151> 2000-09-22

<160> 15

<170> FastSEQ for Windows Version 4.0

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<212> PRT

<213> Homo sapiens

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Gly	Leu	Gly	Gly	Ala	Pro	Leu	Gly	Leu	Arg	Leu	Pro	Arg	Glu	Thr	Asp
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Glu	Glu	Pro	Glu	Glu	Pro	Gly	Arg	Arg	Gly	Ser	Phe	Val	Glu	Met	Val
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Asp	Asn	Leu	Arg	Gly	Lys	Ser	Gly	Gln	Gly	Tyr	Tyr	Val	Glu	Met	Thr
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Val	Gly	Ser	Pro	Pro	Gln	Thr	Leu	Asn	Ile	Leu	Val	Asp	Thr	Gly	Ser
			85						90					95	
Ser	Asn	Phe	Ala	Val	Gly	Ala	Ala	Pro	His	Pro	Phe	Leu	His	Arg	Tyr
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Tyr	Gln	Arg	Gln	Leu	Ser	Ser	Thr	Tyr	Arg	Asp	Leu	Arg	Lys	Gly	Val
	115						120					125			
Tyr	Val	Pro	Tyr	Thr	Gln	Gly	Lys	Trp	Glu	Gly	Glu	Leu	Gly	Thr	Asp
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Leu	Val	Ser	Ile	Pro	His	Gly	Pro	Asn	Val	Thr	Val	Arg	Ala	Asn	Ile
145					150					155				160	
Ala	Ala	Ile	Thr	Glu	Ser	Asp	Lys	Phe	Phe	Ile	Asn	Gly	Ser	Asn	Trp
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Glu	Gly	Ile	Leu	Gly	Leu	Ala	Tyr	Ala	Glu	Ile	Ala	Arg	Pro	Asp	Asp
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Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr His Val Pro
    195                200                205
Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu Asn Gln
    210                215                220
Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly Gly Ile
    225                230                235                240
Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile Arg Arg
    245                250                255
Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn Gly Gln
    260                265                270
Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser Ile Val
    275                280                285
Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe Glu Ala
    290                295                300
Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe Pro Asp
    305                310                315                320
Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly Thr Thr
    325                330                335
Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly Glu Val
    340                345                350
Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr Leu Arg
    355                360                365
Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe Ala
    370                375                380
Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile Met Glu
    385                390                395                400
Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala
    405                410                415
Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala Ala Val Glu
    420                425                430
Gly Pro Phe Val Thr Leu Asp Met Glu Asp Cys Gly Tyr Asn Ile Pro
    435                440                445
Gln Thr Asp Glu Ser Thr Leu Met Thr Ile Ala Tyr Val Met Ala Ala
    450                455                460
Ile Cys Ala Leu Phe Met Leu Pro Leu Cys Leu Met Val Cys Gln Trp
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Arg Cys Leu Arg Cys Leu Arg Gln Gln His Asp Asp Phe Ala Asp Asp
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Ile Ser Leu Leu Lys
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<212> PRT

<213> Homo sapiens

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Gln Ile Ala Met Phe Cys Gly Arg Leu Asn Met His Met Asn Val Gln
    35          40          45
Asn Gly Lys Trp Asp Ser Asp Pro Ser Gly Thr Lys Thr Cys Ile Asp
    50          55          60
Thr Lys Glu Gly Ile Leu Gln Tyr Cys Gln Glu Val Tyr Pro Glu Leu
    65          70          75          80

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Gln	Ile	Thr	Asn	Val	Val	Glu	Ala	Asn	Gln	Pro	Val	Thr	Ile	Gln	Asn
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Ile	Pro	Tyr	Arg	Cys	Leu	Val	Gly	Glu	Phe	Val	Ser	Asp	Ala	Leu	Leu
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Val	Pro	Asp	Lys	Cys	Lys	Phe	Leu	His	Gln	Glu	Arg	Met	Asp	Val	Cys
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Glu	Thr	His	Leu	His	Trp	His	Thr	Val	Ala	Lys	Glu	Thr	Cys	Ser	Glu
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Lys	Ser	Thr	Asn	Leu	His	Asp	Tyr	Gly	Met	Leu	Leu	Pro	Cys	Gly	Ile
			165					170						175	
Asp	Lys	Phe	Arg	Gly	Val	Glu	Phe	Val	Cys	Cys	Pro	Leu	Ala	Glu	Glu
			180					185					190		
Ser	Asp	Asn	Val	Asp	Ser	Ala	Asp	Ala	Glu	Glu	Asp	Asp	Ser	Asp	Val
		195					200					205			
Trp	Trp	Gly	Gly	Ala	Asp	Thr	Asp	Tyr	Ala	Asp	Gly	Ser	Glu	Asp	Lys
	210					215					220				
Val	Val	Glu	Val	Ala	Glu	Glu	Glu	Glu	Val	Ala	Glu	Val	Glu	Glu	Glu
225					230					235					240
Glu	Ala	Asp	Asp	Asp	Glu	Asp	Asp	Glu	Asp	Gly	Asp	Glu	Val	Glu	Glu
			245					250						255	
Glu	Ala	Glu	Glu	Pro	Tyr	Glu	Glu	Ala	Thr	Glu	Arg	Thr	Thr	Ser	Ile
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Ala	Thr	Thr	Thr	Thr	Thr	Thr	Thr	Glu	Ser	Val	Glu	Glu	Val	Val	Arg
	275						280					285			
Val	Pro	Thr	Thr	Ala	Ala	Ser	Thr	Pro	Asp	Ala	Val	Asp	Lys	Tyr	Leu
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Glu	Thr	Pro	Gly	Asp	Glu	Asn	Glu	His	Ala	His	Phe	Gln	Lys	Ala	Lys
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Glu	Arg	Leu	Glu	Ala	Lys	His	Arg	Glu	Arg	Met	Ser	Gln	Val	Met	Arg
			325					330						335	
Glu	Trp	Glu	Glu	Ala	Glu	Arg	Gln	Ala	Lys	Asn	Leu	Pro	Lys	Ala	Asp
			340					345					350		
Lys	Lys	Ala	Val	Ile	Gln	His	Phe	Gln	Glu	Lys	Val	Glu	Ser	Leu	Glu
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Gln	Glu	Ala	Ala	Asn	Glu	Arg	Gln	Gln	Leu	Val	Glu	Thr	His	Met	Ala
	370				375						380				
Arg	Val	Glu	Ala	Met	Leu	Asn	Asp	Arg	Arg	Arg	Leu	Ala	Leu	Glu	Asn
385					390					395					400
Tyr	Ile	Thr	Ala	Leu	Gln	Ala	Val	Pro	Pro	Arg	Pro	Arg	His	Val	Phe
			405					410					415		
Asn	Met	Leu	Lys	Lys	Tyr	Val	Arg	Ala	Glu	Gln	Lys	Asp	Arg	Gln	His
			420					425					430		
Thr	Leu	Lys	His	Phe	Glu	His	Val	Arg	Met	Val	Asp	Pro	Lys	Lys	Ala
		435					440					445			
Ala	Gln	Ile	Arg	Ser	Gln	Val	Met	Thr	His	Leu	Arg	Val	Ile	Tyr	Glu
	450				455					460					
Arg	Met	Asn	Gln	Ser	Leu	Ser	Leu	Leu	Tyr	Asn	Val	Pro	Ala	Val	Ala
465					470					475					480
Glu	Glu	Ile	Gln	Asp	Glu	Val	Asp	Glu	Leu	Leu	Gln	Lys	Glu	Gln	Asn
			485					490					495		
Tyr	Ser	Asp	Asp	Val	Leu	Ala	Asn	Met	Ile	Ser	Glu	Pro	Arg	Ile	Ser
		500						505					510		
Tyr	Gly	Asn	Asp	Ala	Leu	Met	Pro	Ser	Leu	Thr	Glu	Thr	Lys	Thr	Thr
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Val	Glu	Leu	Leu	Pro	Val	Asn	Gly	Glu	Phe	Ser	Leu	Asp	Asp	Leu	Gln

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Pro Trp His Ser Phe Gly Ala Asp Ser Val	Pro Ala Asn Thr Glu Asn			
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Glu Val Glu Pro Val Asp Ala Arg Pro Ala	Ala Asp Arg Gly Leu Thr			560
	565		570	
Thr Arg Pro Gly Ser Gly Leu Thr Asn Ile	Lys Thr Glu Glu Ile Ser			575
	580		585	
Glu Val Lys Met Asp Ala Glu Phe Arg His	Asp Ser Gly Tyr Glu Val			590
	595		600	
His His Gln Lys Leu Val Phe Phe Ala Glu	Asp Val Gly Ser Asn Lys			605
	610		615	
Gly Ala Ile Ile Gly Leu Met Val Gly Gly	Val Val Ile Ala Thr Val			620
625		630		635
Ile Val Ile Thr Leu Val Met Leu Lys Lys	Lys Gln Tyr Thr Ser Ile			640
	645		650	
His His Gly Val Val Glu Val Asp Ala Ala	Val Thr Pro Glu Glu Arg			655
	660		665	
His Leu Ser Lys Met Gln Gln Asn Gly Tyr	Glu Asn Pro Thr Tyr Lys			670
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Phe Phe Glu Gln Met Gln Asn			685	
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<210> 4

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<223> Primer

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29

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<213> Artificial Sequence

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Ser Glu Val Asn Leu Asp Ala Glu Phe Arg
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<213> Homo sapiens

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Gly Tyr Tyr Val Glu Met Thr Val Gly Ser Pro Pro Gln Thr Leu Asn
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Ile Leu Val Asp Thr Gly Ser Ser Asn Phe Ala Val Gly Ala Ala Pro
35 40 45
His Pro Phe Leu His Arg Tyr Tyr Gln Arg Gln Leu Ser Ser Thr Tyr
50 55 60
Arg Asp Leu Arg Lys Gly Val Tyr Val Pro Tyr Thr Gln Gly Lys Trp
65 70 75 80
Glu Gly Glu Leu Gly Thr Asp Leu Val Ser Ile Pro His Gly Pro Asn
85 90 95
Val Thr Val Arg Ala Asn Ile Ala Ala Ile Thr Glu Ser Asp Lys Phe
100 105 110
Phe Ile Asn Gly Ser Asn Trp Glu Gly Ile Leu Gly Leu Ala Tyr Ala
115 120 125
Glu Ile Ala Arg Pro Asp Asp Ser Leu Glu Pro Phe Phe Asp Ser Leu
130 135 140
Val Lys Gln Thr His Val Pro Asn Leu Phe Ser Leu Gln Leu Cys Gly
145 150 155 160
Ala Gly Phe Pro Leu Asn Gln Ser Glu Val Leu Ala Ser Val Gly Gly
165 170 175
Ser Met Ile Ile Gly Gly Ile Asp His Ser Leu Tyr Thr Gly Ser Leu
180 185 190
Trp Tyr Thr Pro Ile Arg Arg Glu Trp Tyr Tyr Glu Val Ile Ile Val
195 200 205
Arg Val Glu Ile Asn Gly Gln Asp Leu Lys Met Asp Cys Lys Glu Tyr
210 215 220
Asn Tyr Asp Lys Ser Ile Val Asp Ser Gly Thr Thr Asn Leu Arg Leu
225 230 235 240
Pro Lys Lys Val Phe Glu Ala Ala Val Lys Ser Ile Lys Ala Ala Ser
245 250 255
Ser Thr Glu Lys Phe Pro Asp Gly Phe Trp Leu Gly Glu Gln Leu Val
260 265 270
Cys Trp Gln Ala Gly Thr Thr Pro Trp Asn Ile Phe Pro Val Ile Ser

	275		280		285										
Leu	Tyr	Leu	Met	Gly	Glu	Val	Thr	Asn	Gln	Ser	Phe	Arg	Ile	Thr	Ile
	290					295					300				
Leu	Pro	Gln	Gln	Tyr	Leu	Arg	Pro	Val	Glu	Asp	Val	Ala	Thr	Ser	Gln
305					310					315					320
Asp	Asp	Cys	Tyr	Lys	Phe	Ala	Ile	Ser	Gln	Ser	Ser	Thr	Gly	Thr	Val
				325					330					335	
Met	Gly	Ala	Val	Ile	Met	Glu	Gly	Phe	Tyr	Val	Val	Phe	Asp	Arg	Ala
			340					345					350		
Arg	Lys	Arg	Ile	Gly	Phe	Ala	Val	Ser	Ala	Cys	His	Val	His	Asp	Glu
			355				360					365			
Phe	Arg	Thr	Ala	Ala	Val	Glu	Gly	Pro	Phe	Val	Thr	Leu	Asp	Met	Glu
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Asp	Cys	Gly	Tyr	Asn	Ile										
385					390										

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<213> Homo sapiens

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		20						25					30		
Leu	Val	Asp	Thr	Gly	Ser	Ser	Asn	Phe	Ala	Val	Gly	Ala	Ala	Pro	His
		35					40					45			
Pro	Phe	Leu	His	Arg	Tyr	Tyr	Gln	Arg	Gln	Leu	Ser	Ser	Thr	Tyr	Arg
	50					55					60				
Asp	Leu	Arg	Lys	Gly	Val	Tyr	Val	Pro	Tyr	Thr	Gln	Gly	Lys	Trp	Glu
65					70					75					80
Gly	Glu	Leu	Gly	Thr	Asp	Leu	Val	Ser	Ile	Pro	His	Gly	Pro	Asn	Val
				85					90					95	
Thr	Val	Arg	Ala	Asn	Ile	Ala	Ala	Ile	Thr	Glu	Ser	Asp	Lys	Phe	Phe
			100					105					110		
Ile	Asn	Gly	Ser	Asn	Trp	Glu	Gly	Ile	Leu	Gly	Leu	Ala	Tyr	Ala	Glu
		115					120					125			
Ile	Ala	Arg	Pro	Asp	Asp	Ser	Leu	Glu	Pro	Phe	Phe	Asp	Ser	Leu	Val
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Lys	Gln	Thr	His	Val	Pro	Asn	Leu	Phe	Ser	Leu	Gln	Leu	Cys	Gly	Ala
145					150					155					160
Gly	Phe	Pro	Leu	Asn	Gln	Ser	Glu	Val	Leu	Ala	Ser	Val	Gly	Gly	Ser
				165					170					175	
Met	Ile	Ile	Gly	Gly	Ile	Asp	His	Ser	Leu	Tyr	Thr	Gly	Ser	Leu	Trp
		180						185					190		
Tyr	Thr	Pro	Ile	Arg	Arg	Glu	Trp	Tyr	Tyr	Glu	Val	Ile	Ile	Val	Arg
		195					200						205		
Val	Glu	Ile	Asn	Gly	Gln	Asp	Leu	Lys	Met	Asp	Cys	Lys	Glu	Tyr	Asn
	210					215					220				
Tyr	Asp	Lys	Ser	Ile	Val	Asp	Ser	Gly	Thr	Thr	Asn	Leu	Arg	Leu	Pro
225					230					235					240
Lys	Lys	Val	Phe	Glu	Ala	Ala	Val	Lys	Ser	Ile	Lys	Ala	Ala	Ser	Ser
				245					250					255	
Thr	Glu	Lys	Phe	Pro	Asp	Gly	Phe	Trp	Leu	Gly	Glu	Gln	Leu	Val	Cys
			260					265					270		
Trp	Gln	Ala	Gly	Thr	Thr	Pro	Trp	Asn	Ile	Phe	Pro	Val	Ile	Ser	Leu

	275					280						285							
Tyr	Leu	Met	Gly	Glu	Val	Thr	Asn	Gln	Ser	Phe	Arg	Ile	Thr	Ile	Leu				
	290						295					300							
Pro	Gln	Gln	Tyr	Leu	Arg	Pro	Val	Glu	Asp	Val	Ala	Thr	Ser	Gln	Asp				
305					310					315					320				
Asp	Cys	Tyr	Lys	Phe	Ala	Ile	Ser	Gln	Ser	Ser	Thr	Gly	Thr	Val	Met				
				325					330					335					
Gly	Ala	Val	Ile	Met	Glu	Gly	Phe	Tyr	Val	Val	Phe	Asp	Arg	Ala	Arg				
			340					345					350						
Lys	Arg	Ile	Gly	Phe	Ala	Val	Ser	Ala	Cys	His	Val	His	Asp	Glu	Phe				
		355					360					365							
Arg	Thr	Ala	Ala	Val	Glu	Gly	Pro	Phe	Val	Thr	Leu	Asp	Met	Glu	Asp				
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Cys	Gly	Tyr	Asn	Ile	Pro														
385					390														

<210> 9
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 <212> PRT
 <213> Homo sapiens

Gly	Ser	Phe	Val	Glu	Met	Val	Asp	Asn	Leu	Arg	Gly	Lys	Ser	Gly	Gln				
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Gly	Tyr	Tyr	Val	Glu	Met	Thr	Val	Gly	Ser	Pro	Pro	Gln	Thr	Leu	Asn				
			20					25				30							
Ile	Leu	Val	Asp	Thr	Gly	Ser	Ser	Asn	Phe	Ala	Val	Gly	Ala	Ala	Pro				
		35				40					45								
His	Pro	Phe	Leu	His	Arg	Tyr	Tyr	Gln	Arg	Gln	Leu	Ser	Ser	Thr	Tyr				
	50				55					60									
Arg	Asp	Leu	Arg	Lys	Gly	Val	Tyr	Val	Pro	Tyr	Thr	Gln	Gly	Lys	Trp				
65				70				75						80					
Glu	Gly	Glu	Leu	Gly	Thr	Asp	Leu	Val	Ser	Ile	Pro	His	Gly	Pro	Asn				
			85					90					95						
Val	Thr	Val	Arg	Ala	Asn	Ile	Ala	Ala	Ile	Thr	Glu	Ser	Asp	Lys	Phe				
			100				105						110						
Phe	Ile	Asn	Gly	Ser	Asn	Trp	Glu	Gly	Ile	Leu	Gly	Leu	Ala	Tyr	Ala				
		115				120					125								
Glu	Ile	Ala	Arg	Pro	Asp	Asp	Ser	Leu	Glu	Pro	Phe	Phe	Asp	Ser	Leu				
	130				135					140									
Val	Lys	Gln	Thr	His	Val														
145					150														

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 <213> Homo sapiens

Pro	Asn	Leu	Phe	Ser	Leu	Gln	Leu	Cys	Gly	Ala	Gly	Phe	Pro	Leu	Asn				
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Gln	Ser	Glu	Val	Leu	Ala	Ser	Val	Gly	Gly	Ser	Met	Ile	Ile	Gly	Gly				
		20					25					30							
Ile	Asp	His	Ser	Leu	Tyr	Thr	Gly	Ser	Leu	Trp	Tyr	Thr	Pro	Ile	Arg				
		35				40						45							

Arg	Glu	Trp	Tyr	Tyr	Glu	Val	Ile	Ile	Val	Arg	Val	Glu	Ile	Asn	Gly
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Gln	Asp	Leu	Lys	Met	Asp	Cys	Lys	Glu	Tyr	Asn	Tyr	Asp	Lys	Ser	Ile
65					70					75				80	
Val	Asp	Ser	Gly	Thr	Thr	Asn	Leu	Arg	Leu	Pro	Lys	Lys	Val	Phe	Glu
				85					90					95	
Ala	Ala	Val	Lys	Ser	Ile	Lys	Ala	Ala	Ser	Ser	Thr	Glu	Lys	Phe	Pro
			100					105					110		
Asp	Gly	Phe	Trp	Leu	Gly	Glu	Gln	Leu	Val	Cys	Trp	Gln	Ala	Gly	Thr
		115					120					125			
Thr	Pro	Trp	Asn	Ile	Phe	Pro	Val	Ile	Ser	Leu	Tyr	Leu	Met	Gly	Glu
	130					135					140				
Val	Thr	Asn	Gln	Ser	Phe	Arg	Ile	Thr	Ile	Leu	Pro	Gln	Gln	Tyr	Leu
145					150					155					160
Arg	Pro	Val	Glu	Asp	Val	Ala	Thr	Ser	Gln	Asp	Asp	Cys	Tyr	Lys	Phe
				165					170					175	
Ala	Ile	Ser	Gln	Ser	Ser	Thr	Gly	Thr	Val	Met	Gly	Ala	Val	Ile	Met
			180					185					190		
Glu	Gly	Phe	Tyr	Val	Val	Phe	Asp	Arg	Ala	Arg	Lys	Arg	Ile	Gly	Phe
		195					200				205				
Ala	Val	Ser	Ala	Cys	His	Val	His	Asp	Glu	Phe	Arg	Thr	Ala	Ala	Val
	210					215				220					
Glu	Gly	Pro	Phe	Val	Thr	Leu	Asp	Met	Glu	Asp	Cys	Gly	Tyr	Asn	Ile
225					230					235					240

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<213> Homo sapiens

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Pro	Tyr	Thr	Gln	Gly
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Ser Ser Thr Gly
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